Concordance between the Wada test and neuroimaging lateralisation: influence of imaging modality (fMRI and MEG) and patient experience

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ABSTRACT

The Wada test remains the traditional test for lateralising language and memory function prior to epilepsy surgery. Functional imaging and particularly fMRI has made progress in the language domain, but less so in the memory domain. MEG has received less research attention, but shows promise, particularly for language lateralization. We recruited a consecutive sample of 19 patients with epilepsy who had completed pre-surgical work-up, including the Wada test, and compared fMRI (memory) and MEG (language and memory) with Wada test results. The main research question was the concordance between Wada and these two imaging techniques as pre-epilepsy surgery investigations. We were also interested in the acceptability of the three techniques to patients. Concordance rates (N=16) were non-significant (Cohen's Kappa) between fMRI and Wada test (memory) and between MEG and Wada test (memory and language). The Wada test was a well-established protocol used at several epilepsy surgery centres in the UK. Patients generally found the Wada test an odd, but not aversive procedure. Sixteen (84%) patients who were scanned reported some level of obtundation in MEG. We present these discordant findings in support of the position that functional imaging and the Wada test are distinctive procedures, with little in the way of overlapping mechanisms, and that patient's experience should be taken into account when procedures are selected and offered to them.

Key words: Wada test, functional MRI (fMRI), magnetoencephalography(MEG), laterality, memory, language.

1. Introduction

Resective surgery for medically intractable focal epilepsy remains an effective procedure for many patients and is considered to be under-utilised [1]. In the context of preoperative evaluation, the Wada test (i.e. intracarotid amobarbital procedure) has been routinely used by many centres around the world to establish hemispheric language and memory function [2,3,4]. The past decade has seen considerable research interest in replacing the Wada test with non-invasive neuroimaging techniques including functional MRI (fMRI) and magnetoencephalography (MEG), among others (e.g. functional transcranial Doppler sonography) [5,6,7]. This shift in research emphasis is laudable and driven by the medical risks associated with the invasive Wada test [8,9], the nature of Wada testing being resource-intensive and costly, the limited availability of sodium amytal and the increasing availability of fMRI and MEG in epilepsy surgery centres [2,8,9].

Previous work from our own centre [10] showed that a subgroup of patients with specific clinical characteristics (i.e. right-handed patients, with right temporal lobe lesions with intact verbal memory) had a zero base-rate of Wada test failure. We made a case for using the Wada test on a selective basis. Baxendale [2] examined the indicators for conducting a Wada test and concluded that although decisions should be taken on a case-by-case basis, patients at high-risk of memory decline could be identified using structural and functional imaging together with neuropsychological testing and clinical variables. In a recent survey of 115 epilepsy professionals, mainly epileptologists, it was reported that 100% of those from Europe and 75% from North America indicated that the Wada test was not necessary [11]. Furthermore, Papanicolaou et al. [7] made a case for replacing the Wada test, and cortical stimulation mapping, as the method of choice, in many if not most cases, using fMRI / MEG.

It is interesting to consider how this apparent shift in clinical opinion and research emphasis fits with the literature on the concordance between fMRI / MEG and Wada test results. In a recent meta-analysis of fMRI and Wada test concordance for pre-operative language lateralisation, Bauer et al [5] included 22 studies on 504 patients.

Overall, fMRI was concordant with Wada in 406 patients (80.5%) and discordant in 98 patients (19.5%). fMRI and Wada agreed in 94% in those patients with typical language lateralisation and agreed in just 51% with atypical language representation. The authors conclude that fMRI is a suitable triage test and that Wada testing is probably indicated when fMRI does not establish clear left lateralisation. Janecek et al [12] compared fMRI and Wada language lateralisation in 229 patients using semantic decision making fMRI protocol. Discordant results were found in 14% of patients and were highest among patients categorised by either test as having bilateral language. Lopes et al [13] developed an easy version of a semantic decision making task that could be used with a wide range of patients, including children and adults with cognitive deficits. They found that both an easy version and a more complex semantic decision making task was useful for language lateralisation. There were common areas of brain activation between the 'easy' and 'complex' versions, with the complex version producing greater activation in the left superior and middle frontal giri, angular gyrus and left posterior cingulate gyrus.

In terms of fMRI and memory, Limotai and Mirsattari [14] reviewed the literature on the pre-surgical work-up for temporal lobe epilepsy surgery, and located nine studies utilising different fMRI memory paradigms. Most of these studies showed memory asymmetry with fMRI to be concordant to the memory findings with the Wada test. One study [15] showed marked discordance between Wada and memory activations using scene encoding and recognition on 14 right and 11 left lesion patients. Concordance was 48% using a pooled measure of fMRI memory activations, and the concordance did not improve when Wada laterality index was compared to individual memory conditions. The authors concluded that based on the existing literature, although promising, fMRI cannot replace the Wada test for routine pre-surgical evaluation of memory. A more recent review and practice guidelines for the use of fMRI in pre surgical evaluation is provided by Szaflarski et al [16]. In terms of whether fMRI is comparable with Wada for language lateralization, the authors conclude that fMRI possibly provides language lateralisation concordant with the Wada test in 87% of medial temporal lobe epilepsy and 81% of extra temporal cases. In terms of whether fMRI is comparable with Wada for measuring memory lateralization, they conclude that fMRI may be considered as an option to lateralise language and highlight one study [15] showing discordant findings.

Fewer studies exist on concordance between MEG and Wada, but these data generally support the position that concordance between the two techniques for language is generally high, although variable in terms of the imaging language paradigm used [17]. Less is known about the concordance between MEG and memory. It is recognised that MEG has certain technical and clinical advantages over fMRI and is portrayed as a potential future application for the lateralisation of memory function [18].

The past decade has seen a shift in clinical and research interest away from the Wada test as a method of pre-surgical risk prediction to non-invasive brain imaging techniques. However, there is variance in the imaging research literature and no one imaging technique or activation paradigm has come to prominence. There is possibly over-enthusiasm for imaging alternatives to the Wada test and a need for further evaluation and finessing of non-invasive methods, particularly for memory. To this end, we conducted a study comparing MEG (language and memory) activations with Wada test findings, and fMRI (memory) activations with Wada test results. The main research question was the concordance between these three techniques, with the Wada test as the traditional gold standard. We were also interested in the acceptability of these three procedures to patients.

2. Methods

2.1. Participants

A consecutive series of 19 adult patient undergoing work-up for temporal lobectomy for the relief of epilepsy at two UK epilepsy surgery centres were recruited prospectively. Wada testing was done as the final investigation prior to surgery and patients agreeing to participate in the study underwent two additional scans (fMRI and MEG prior to surgery) at the York Neuroimaging Centre (YNiC). Patients were invited to participate in the study after Wada testing, which was typically two to three months prior to epilepsy surgery. Three patients declined to participate in the study, two patients because of feeling anxious about surgery and not wanting further tests. One patient declined because of claustrophobia in the MRI scanner. Nineteen patients were recruited to the study and scanned. Six sets of MEG data were

unusable due to signal artefacts and three sets of fMRI data were unusable for technical reasons. Table 1 reports the clinical and demographic data on 16 participants. Fourteen participants were right-handed and two left-handed. Most participants had hippocampal sclerosis (N=11; 68%), with the remainder having dysembryoplastic neuroepithelial tumours (DNET) or glioma. Twelve patients had left-sided lesions and four had right-sided lesions. All lesions were in the temporal lobe. All patients were considered amenable to surgery and all suffered from refractory seizures having failed on at least three anti-epileptic drugs. Diagnostic MRI imaging was reported by a consultant neuroradiologist and lateralising and localising features on video EEG reported by a consultant neurophysiologist. All patients had undergone baseline neuropsychological testing and no patients recruited in this consecutive series had a learning disability. All patients were discussed at MDT meetings prior to Wada testing at respective epilepsy surgery centres. The study was granted permission from a University Teaching Hospital research ethics committee.

All patients underwent the MEG and fMRI scanning during a single session. We used a single language paradigm to reduce scanning time.

Insert Table 1 about here

2.2. Wada test

The Wada test procedure used was previously published by Kemp et al [10]. The protocol was developed at four centres in the north of England, including the two centres involved in the present study. The procedure is led by a consultant clinical neuropsychologist and patients are well prepared psychologically. Patients have angiography to position the catheter in the internal carotid artery prior to injection. In addition, all patients undergo EEG monitoring throughout. The hemisphere ipsilateral to the side of proposed surgery is injected first (thus enabling memory capacity of the hemisphere contralateral to the side of surgery to be tested first). Sodium amytal is titrated slowly, the injection being stopped on signs of EEG slowing and contralateral hemiparesis. The dose is typically in the range 80–120 mg. Language functioning is tested first. Comprehension is assessed by asking the

patient to follow some simple commands. Speech is then assessed by asking the patient to verbalize some basic information. Speech is further assessed by presenting a picture of a complex scene and asking the patient to verbalize the details. Six memory items are then presented visually. This element of the procedure typically lasts three minutes or less. The patient is then left to rest, supported by a specialist epilepsy nurse and monitored by medical staff. The effect of the sodium amytal is judged to have worn off when the EEG returns to the pre-injection baseline and the patient can demonstrate equal bilateral grip strength. Memory is then tested by free recall and recognition for the six items presented during the injection phase (free recall = two points / recognition choice = one point). Patients unable to free recall any of the 6 items are given a visual recognition trial comprising 4 items (the stimulus item and 3 foils). This allows a maximum score of 12 points. The cut-off point is six points, with any score below that being classed as a fail. The chance level of responding is 1.5/12. The choice of cut-off was a pragmatic decision based on well-above-chance performance. We acknowledge that the cut-off and scoring criteria will affect the results and that our protocol is different from that of other institutions. After testing, patients are asked about their subjective experience of the procedure. The procedure is filmed to enable responses to be checked prior to discussing the results with patients. After a 45-min delay, deactivation of the hemisphere contralateral to the side of surgery is then carried out and the procedure is repeated with alternative stimuli.

2.3. MEG language and memory testing

MEG scanning was performed at York Neuroimaging Centre, University of York, using a 4D Neuroimaging Magnes 3600 Whole Head 248 Channel MEG scanner. Data were recorded at a sample rate of 678.17 Hz and were bandpass filtered online between 1 and 200 Hz using a finite impulse response (FIR) filter. Previous to the recording, a Polhemus Fastrak System was used for the spatial co-registration of individual facial and scalp landmarks (left and right preauricular points, Cz, nasion and inion). The landmark locations in relation to the sensor positions were determined based on a precise localization signal produced by five spatially distributed head coils with a fixed spatial relation to the landmarks. Using these head coils, we were able to measure each participant's head movement at the beginning

and end of each scan. To carry out artefact rejection, the raw data from each epoch were inspected visually and epochs contaminated with either physiological or non-physiological artefacts were manually removed.

For the source-space analyses, the landmark locations were matched with the individual participants' anatomical MRI scans using a surface-matching technique adapted from Kozinska et al. [19] (see functional MRI methods for MRI acquisition parameters). Co-registration to the MNI standard space was performed by a linear transform implemented using FLIRT [20] from the FMRIB Software Library (https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FLIRT).

We utilized three MEG tasks: verb generation, verbal memory and non-verbal memory. For verb generation, 150 stimuli (nouns) were presented in three blocks of 50 words. The same 50 words were used in each block with different randomisation. The participant determined the break between each block length. Stimulus presentation duration lasted two seconds and inter-stimulus interval was 1100 - 1600 ms. Participants were asked to think of an action associated with the word, but not verbalise their responses (e.g. If you see the word ‘airplane’ - you could think the word ‘fly’). For verbal and non-verbal memory tasks, 150 stimuli were presented in three blocks of 50, again using 50 unique stimuli. At the end of each encoding block (50 stimuli), there was a retrieval stage consisting of eight stimuli. The 8 stimumi were presented sequentially (one at a time) with the same timings as for the encoding stage. Upon seeing the stimulus the participants were required to press a button if they had seen the stimulus in the previous encoding block. Four out of 8 of the stimuli were novel and not seen before. This was a way of ensuring that the participants were engaging with the task, but there were insufficient repetitions to be able to quantify performance. Stimulus presentation duration lasted 2.5 seconds, and inter stimulus interval was 1000 ms.

We used two approaches for the analysis of MEG data: Beamformer and Dipole fitting. All MEG data pre-processing and analyses were performed using NeuroImaging Analysis Framework (NAF), an open-source, python-based set of tools for analysing MEG data (https://vcs.ynic.york.ac.uk/naf/naf).

2.3.1. (i) Beamformer

Neural sources of activity [21,22] were reconstructed using a Type I beamformer [23] with a multiple-spheres head model [24]. A grid of points was placed throughout the cortical volume, with a spatial resolution of 5 mm. Two contiguous analysis windows were used for all three tasks. The one defined as "Active" was set from 0 to 500 ms post-stimulus-onset and the second one named "Passive" from -500 ms to 0 pre-stimulus-onset. These were compared using a broadband filter (1–80 Hz). A two-sample paired t-test was then performed for each voxel, at the individual level and for each task. The resulting t-values showed changes in power in the active window against the passive baseline window.

In order to calculate a laterality index (LI) for each task per subject, we focused on voxels showing peak activity (local maxima) throughout the whole-brain, excluding the occipital lobe and the cerebellum. Up to ten local maxima were selected in each case and the LI was then defined as:

$$LI = 100 \times \frac{L - R}{L + R}$$

where L represents the summed t-values of all peak voxels in the left hemisphere and R represents the summed t-values of all peak voxels in the right hemisphere.

2.3.2. (ii) Dipole fitting

Aiming to explore how a different source localisation approach might influence the laterality outcomes in each task, we also performed our source space analysis by calculating an Equivalent Current Dipole (ECD) that best fitted the observed MEG data. Epochs of interest were defined from -500 to 1500 ms with respect to the stimulus onset. After calculating the mean epoch activity for all MEG channels, a dipole (non-radial orientation, 5 mm grid spacing) was fitted every 4 ms starting at stimulus onset up to 500 ms using data from 31 channels with the highest absolute magnetic flux measurements. Dipoles were considered reliable if they had a correlation coefficient R > 0.9 and a goodness of fit > 0.9, otherwise they were

rejected. Based on the hemispheric location of the remaining dipoles, the LI for each task and each participant was also defined as:

$$LI = 100 \times \frac{L - R}{L + R}$$

where L represents the number of dipoles in the left hemisphere and R represents the number of dipoles in the right hemisphere.

2.4. Memory fMRI

fMRI data were also acquired at York Neuroimaging Centre using an eight-channel phased array head coil (GE) tuned to 127.4MHz on a GE 3 Tesla Signa Excite HDxMRI scanner. A single-shot pulsed gradient spin-echo echo-planar imaging (EPI) sequence was used with the following parameters: scan duration 16 min, 320 volumes, TR 3000 ms, TE ≈ 40 ms, flip angle 90°, voxel size 2.25 x 2.25 x 3 mm^3, matrix 128 x 128, FOV 288 x 288 mm^2, slice thickness 3 mm, 36 slices and an interleaved (bottom up) acquisition order. We additionally acquired sagittal isotropic 3D fast spoiled gradient-recalled echo (3D FSPGR) structural T1 weighted images for each participant with the following acquisition parameters: TR = 7.8 ms, TE = minimum full, flip angle = 20°, matrix size = 256 x 256, voxel size = 1.13 x 1.13 x 1 mm^3, FOV = 289 x 289 mm^2.

To assess memory lateralisation, we used a memory encoding paradigm. Complex visual scenes were used, which consisted of photographs of buildings, parks, spaces and landscapes from around the world. Each image was presented for 3400 ms with an inter-stimulus interval of 500 ms. A block design was used with ten images presented in an encoding block, which was followed by a control block consisting of scrambled images. Each block was therefore 39 seconds in total and the acquisition consisted of 12 full blocks of encoding and control stimuli.

The functional data were co-registered with the structural T1-weighted images. To facilitate the co-registrations, a high-resolution T1-weighted in-plane anatomical image was also acquired for all participants, using a fluid attenuated inversion

recovery (FLAIR) sequence with parameters TR = 2320 ms, TE = 9.9 ms and TI = 1050 ms and the same slice prescription as the fMRI acquisitions. All fMRI pre-processing and analyses were performed using FSL software (http://fsl.fmrib.ox.ac.uk; v4.1.9). We extracted the brain from the skull using the Brain Extraction Tool (BET) [25] for both the FLAIR and the structural T1-weighted images and linearly registered them to MNI standard space using FLIRT [20] . The following pre-processing was applied to the functional data; motion correction using MCFLIRT [20], slice-timing correction using Fourier-space time-series phase shifting, non-brain removal using BET, spatial smoothing using a Gaussian kernel of FWHM 6mm, grand-mean intensity normalisation of the entire 4D dataset by a single multiplicative factor, and high pass temporal filtering (Gaussian-weighted least-squares straight line fitting, with sigma = 40 s). Time-series statistical analysis was carried out using FILM with local autocorrelation correction [26].

Our aim was to evaluate activations as represented by increases in BOLD response during the encoding phase. This condition was modelled using the General Linear Model after convolution with a single-gamma Hemodynamic Response Function. Six motion parameters calculated in the motion-correction step during pre-processing were also included as nuisance regressors for each individual. The resulting contrast images showed differences in brain activity during the encoding blocks compared to the control blocks and were thresholded at the whole-brain level using GRF-theory-based maximum height thresholding with a (corrected) significance threshold of p = 0.05 [27]. The LI was based on the z-values of voxels showing a significant increase in brain activity during the encoding blocks compared to the control blocks and it was defined as:

$$LI = 100 \times \frac{L - R}{L + R}$$

where L represents the summed z-values of voxels in the left hemisphere and R represents the summed z-values of voxels in the right hemisphere. Voxels in the occipital lobe and the cerebellum were excluded.

3. Results

The relationship between MEG and Wada findings on hemispheric dominance for each participant and each task is presented in Table 2, 3 and 4 respectively. For the memory tasks, hemispheric dominance was declared upon a >2 point difference in the Wada memory score for each participant, otherwise it was characterised as bilateral.

For all laterality indices (LI), positive values indicated left hemispheric activation was greater than right, and negative values indicate that right hemispheric activation was greater than left. For each participant and each task, a LI score ≥ 10 was considered indicative of left-hemisphere dominance, a value ≤ −10 indicative of right-hemisphere dominance and a value between −10 and 10 was considered bilateral.

For MEG verb generation, there was an agreement of 46.2% for the beamformer analysis and 61.5% for the Dipole approach (Table 2). The respective agreement values were 61.5%, and 23.1% for MEG verbal memory (Table 3), and 46.2%, and 38.5% for MEG non-verbal memory (Table 4).

Concordance between fMRI and Wada for memory encoding is presented in Table 5. Concordance between Wada laterality and fMRI laterality analysis was 31.3%.

Insert Tables 2,3,4,5 about here

Concordance rates were non-significant (Cohen's Kappa) for both memory and language between fMRI and MEG compared to the Wada test protocol.

All participants were asked whether the experience of the three procedures was acceptable. All participants found MEG acceptable, but 16 (84%) of the 19 participants scanned reported some level of obtundation in the MEG scanner. No

participant had undergone MEG scanning before. All participants had prior experiences of MR scanning, but none that included fMRI. All 19 patients found fMRI acceptable, but eight (42%) patients commented that they spent longer in the scanner than with prior structural MR scans. All patients expressed some anxiety about Wada testing and, as per the epilepsy surgery protocol, were carefully prepared for the procedure by the consultant clinical neuropsychologist. All patients found the Wada test to be an unusual, but not particularly aversive experience.

4. Discussion

We addressed the concordance between fMRI and Wada test (memory) and MEG and Wada test (memory and language) in a prospective cohort of 19 adult patients with temporal lobe lesions prior to epilepsy surgery recruited from two centres in the UK. Certain imaging data were unusable. We were also interested in the acceptability of these three techniques to patients.

Using a verb generation task, 46% to 61% of participants had concordant MEG and Wada test findings. These concordance rates are lower than those typically reported for language comprehension and language production paradigms with MEG (see [7,17] for a summary). However, not all of these studies assessed adult patients with intractable epilepsy. Further, using a semantic word-processing task, Tanaka et al. [28] reported that the concordance between MEG and the Wada test depended on the method of analysis. In particular, they report a dynamic statistical parametric mapping (dSPM) ‘counting’ method, based on the number of unit dipoles with activation over a threshold in regions-of-interest, yielded substantially higher consistency between approaches compared to a dSPM ‘amplitude’ method that is based on the amplitude of activation in the regions-of-interest. The dSPM-counting method demonstrated laterality with Wada in 91.4% of patients, whereas, the dSPM-amplitude method showed 51.4% concordance. Although language has received more research attention than memory activations with MEG, there is no consensus on, which tests to use with pre-surgical epilepsy [29].

Using a verbal and non-verbal memory encoding task, we found 61.5% and 46.2% of patients respectively to have MEG activations concordant with Wada LI. Fewer

studies have looked at the concordance between MEG and memory. In 2010, Ray & Bowyer [18] addressed the clinical applications of MEG in epilepsy and concluded that lateralization of memory function is a potential future application. Little progress has been made since 2010. Pirmoradi et al [29] report higher concordance rates between a verbal memory paradigm and language dominance in controls (using handedness as criterion) and in patients with epilepsy (using fMRI or Wada as criterion), compared to a verbal fluency task. Only the concordance for verbal memory reached statistical significance, with 93% agreement.

We used a single memory test during fMRI (encoding of complex scenes) and based on earlier work [30] we anticipated bilateral activation. Functional MRI scanning was limited to a single paradigm because memory is the more difficult and pressing question, and also we sought to keep total scanning time down to a minimum. We found that Wada test memory asymmetry and LI in fMRI were concordant in 31.3% of patients. This finding is lower than most of the concordance rates reported by Limotai and Mirsattari [14] on their review of the literature on fMRI and Wada for memory, but in keeping with the findings of Dupont et al [15]. Most of the relevant literature has looked at replacing the Wada test for language lateralisation rather than memory. In terms of memory, most studies have looked at predicting post-operative memory outcome rather than comparing functional imaging with Wada test findings. Of the relatively small number of studies that have looked at the concordance between fMRI and Wada for memory laterality, the present data add to the discordant findings.

These data have certain limitations. We recruited from a cohort of patients under the care of epilepsy surgery programmes at various centres, with patients invited to undergo the research scans at the end serial routine investigations just prior to surgery. We recruited and scanned 19 patients, but lost 9 sets of imaging data in total on technical grounds. Although the N=16 that we report is modest, these patients had uncomplicated Wada test findings and both MEG and MRI / fMRI data sets. The modest sample size does limit the generalizability of our findings. Whilst we excluded imaging (MEG and fMRI) data with technical difficulties and used a shared regional Wada test protocol that the centres had many years' experience with, it cannot be assumed that the Wada test is correct in every case, nor that our

imaging findings are incorrect in every discordant case. On a more conceptual level, it is reasonable to ask whether the need for the Wada test is best evaluated by concordance between the procedure and functional imaging paradigms. Other groups have taken different approaches. To identify patients at risk of post-operative memory decline, Binder et al [31, 32] used pre-operative fMRI hippocampal activations to predict change in pre to post-operative memory test scores. Baxendale [2] proposed a multivariate risk appraisal model to identify patients at high risk of post-operative memory decline and propose that the Wada test should be used on a case-by-case basis.

In summary, we addressed the questions of whether MEG language and memory tasks were comparable with Wada for measuring language and memory lateralization, and whether an fMRI memory task was comparable with Wada for memory lateralization. We were also interested in the acceptability of these three procedures (MEG, fMRI and Wada) to patients. We report a range of non-significant (Cohen's Kappa) concordance rates between 61.5% and 31.3% and conclude that an fMRI scene encoding tasks is not concordant with Wada memory testing and not an acceptable replacement for the Wada test. Likewise, we conclude that a verb generation task and two memory tasks (list learning and designing learning) are not concordant with Wada language and memory results and not an acceptable replacement for Wada testing. Such discordant findings are not unprecedented in the literature. We present these findings as a caution to viewing functional imaging as a replacement for Wada testing and in the context of a relatively small literature that has yet to establish consensus on, which imaging technique, which activation paradigms and, which method of analysis to best apply clinically. These data support the position taken by Limotai and Mirsattari [14] that imaging technology is yet to attain its full potential and the position taken by Połczyńska et al [33] that imaging and the Wada test may turn out to be complementary and not competing techniques to counsel and safeguard patients from adverse neuropsychological outcomes following epilepsy surgery.

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Table 1: Demographic and clinical data for 16 patients

Patient number	Age / gender	handed	Lesion type	Lesion location	Language dominance
1	48 / F	R	Hippocampal sclerosis	L	L
2	22 / F	R	Hippocampal sclerosis	L	Bi-lateral
3	34 / M	R	Hippocampal sclerosis	L	L
4	47 / M	R	Hippocampal sclerosis	L	L
5	47 / M	R	Hippocampal sclerosis	L	L
6	38 / F	R	Low grade glioma	L temporal	L
7	42 / M	R	Hippocampal sclerosis	R	L
8	34 / M	R	DNET	L temporal	L
9	42 / M	R	Low grade glioma	L Temporal	L
10	46 / M	R	Hippocampal sclerosis	L	L
11	43 / F	R	Hippocampal sclerosis	R	L
12	18 / M	L	temporal/hippocampal mass ? Ganglioglioma	L	R
13	53 / M	R	Hippocampal sclerosis	R	L
14	35 / M	R	DNET	R temporal	L
15	26 / F	L	Hippocampal sclerosis	L	L
16	45 / F	R	Hippocampal sclerosis	R	L

Table 2: MEG Wada concordance for verb generation

Participant	WADA	LI Beamformer	LI Dipole
1	Left	Left	Left
2	Bilateral	Right	Left
3	Left	Left	Left
4	Left	Bilateral	Left
5	Left	Bilateral	Left
6	Left	Bilateral	Left
7	Left	Left	Left
8	Left	Bilateral	N/A
9	Left	Left	Left
10	Left	Left	Left
11	Left	Left	Right
12	Right	Left	Left
13	Left	Right	Right
		Agreement %	
		46.2	61.5

Table 3: MEG Wada concordance for verbal memory

Participant	WADA	LI Beamformer	LI Dipole
1	Left	Left	Right
2	Right	Right	Left
3	Bilateral	Left	Left
4	Bilateral	Bilateral	Left
5	Bilateral	Right	Left
6	Left	Bilateral	Left
7	Left	Left	Right
8	Left	Left	Right
9	Right	Left	N/A
10	Right	Right	Right
11	Left	Right	Right
12	Right	Right	Left
13	Left	Left	Left
		Agreement %	
		61.5	23.1

Table 4: MEG Wada concordance for non-verbal memory

Participant	WADA	LI Beamformer	LI Dipole
1	Left	Right	Left
2	Right	Right	Left
3	Bilateral	Left	Left
4	Bilateral	Bilateral	Left
5	Bilateral	Right	Left
6	Left	Left	Left
7	Left	Left	Right
8	Left	Right	N/A
9	Right	Right	Right
10	Right	Bilateral	Left
11	Left	Right	Left
12	Right	Right	Right
13	Left	Bilateral	Bilateral
		Agreement %	
		46.2	38.5

Table 5: fMRI Wada concordance for memory encoding (complex scenes)

Participant	WADA	LI fMRI
1	Left	Bilateral
2	Right	Bilateral
3	Bilateral	Left
4	Bilateral	Left
5	Bilateral	Bilateral
6	Left	Right
7	Left	Bilateral
8	Left	Bilateral
9	Right	Right
10	Right	Bilateral
11	Left	Left
12	Right	Right
13	Left	Bilateral
14	Left	Bilateral
15	Right	Bilateral
16	Right	Right
		Agreement %
		31.3